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New Study Shows Florbetapir F 18 Injection Scans Led to Change in Diagnosis and Management of Patients Being Evaluated for Cognitive Decline

Study Results Presented at the Alzheimer's Association International Conference® 2015

INDIANAPOLIS, July 22, 2015 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) and Avid Radiopharmaceuticals, Inc., a wholly owned subsidiary of Lilly, today announced new data showing that knowledge of amyloid status as determined by Florbetapir F 18 Injection imaging altered diagnosis and management in the majority of patients being studied. This is the first study to look at the impact of amyloid imaging on diagnosis and actual patient management using a randomized, controlled prospective design.¹ These findings were presented today at the Alzheimer's Association International Conference® 2015 (AAIC®) in Washington, D.C.

The presence of beta-amyloid neuritic plaque in the brain may provide additional information to supplement a physician's clinical assessment of a patient with cognitive impairment. However, a negative beta-amyloid imaging scan indicates sparse to no plaques are currently present, which is inconsistent with a neuropathological diagnosis of Alzheimer's disease and reduces the likelihood that a patient's cognitive impairment is due to the disease.² It is important to note that errors may occur during image interpretation. Also, a positive scan does not establish a diagnosis of Alzheimer's disease or other cognitive disorders and a negative scan does not preclude the development of brain amyloid in the future.

"These study results are the first to suggest in a controlled study that adding florbetapir to the diagnostic evaluation changed actual patient diagnosis and management by physicians who regularly manage this complicated and devastating disease," said Michael Pontecorvo, Ph.D., vice president, clinical development, Avid Radiopharmaceuticals, a wholly owned subsidiary of Lilly. "Alzheimer's disease is one of many possible causes of cognitive impairment, which can make diagnosis challenging. These findings provide further support for how knowledge of the presence or absence of amyloid pathology may affect both diagnosis and management in patients being evaluated for Alzheimer's disease or other possible causes of cognitive decline."

In addition to altering patient diagnosis, results showed that knowledge of amyloid status as determined by florbetapir imaging changed patient management in the majority of study patients, particularly Alzheimer's disease medications (cholinesterase inhibitor use), in a direction consistent with amyloid status. The researchers found no group differences in cognitive performance or health outcomes at one year, and changes in medical history, psychotropic drug use, and psychiatric-related events were not significantly different between the immediate and delayed feedback groups. There was no evidence of increased safety risk associated with early disclosure of amyloid status.¹

These data add to a growing body of work that suggests knowledge of amyloid status may change intended and actual patient management.^{3,4,5}

Study Methods¹

The goal of this multicenter study was to evaluate the impact of amyloid positron emission tomography (PET) on patient management and outcomes in a randomized, controlled setting. After identifying patients seeking diagnosis for mild impairment or dementia, where Alzheimer's disease was considered a possible cause (< 85 percent certain), physicians recorded a working diagnosis and management plan. Patients underwent a florbetapir PET scan and were then randomized to either immediate or delayed (one year) feedback groups regarding amyloid status.

When patients returned to the center after three months, the physician updated the diagnosis and recorded an actual management summary. Patients then returned to the center one year post baseline for assessment of patient and caregiver outcomes including change in cognitive status (ADAS-Cog), health outcomes/resource utilization, mood, function and quality of life. The pre-specified primary analyses examined the impact of immediate feedback versus delayed feedback of amyloid status on diagnosis and management changes at three months.

A total of 618 subjects were randomized to the immediate (308) or to the delayed (310) amyloid PET feedback arms, including 174 subjects in France, 221 in Italy and 223 in the United States. Six hundred and two subjects completed the three month and 560 completed the one year follow-up visits.

Key Results Details¹

- The percentage of patients with management changes was higher in the immediate feedback group compared to the delayed feedback group (68.0 percent versus 56.0 percent)
 - This difference was driven mainly by Alzheimer's disease medication changes, particularly cholinesterase inhibitor use, when patients were sorted by amyloid status
 - In the immediate feedback group, cholinesterase inhibitor use increased in amyloid positive subjects and decreased in amyloid negative subjects so that 67.0 percent of amyloid positive versus only 27.0 percent of amyloid negative subjects were receiving medications three months after scan
 - In contrast, in the delayed feedback group, Alzheimer's disease medication use increased regardless of amyloid status such that 56.0 percent amyloid positive and 43.0 percent amyloid negative subjects were receiving cholinesterase inhibitors
- Results suggested that knowledge of amyloid status as determined by florbetapir imaging changed actual patient diagnosis (32.6 percent in the immediate feedback group compared to 6.4 percent in the delayed feedback group)
 - Of note, diagnosis change among cases with contradicting initial diagnosis versus scan results was 85.6 percent for the immediate feedback group compared to 11.9 percent for the delayed feedback group
- There were no group differences in cognitive performance or health outcomes at one year as measured by the following:
 - Cognitive change from baseline (ADAS, MMSE, FAQ)
 - Resource use on the RUD
 - Quality of life on the QoL AD
 - Caregiver Self Efficacy

Study limitations included:

- Physicians frequently failed to perform the diagnostic and neuropsychology tests and follow-up visits that were a part of their pre-scan management plan
- The study was not designed to assess health outcomes impact
- The trial reflects current physician behavior and available treatments. Results could change with physician education and experience with amyloid PET scans, and with the advent of new medications

About Amyvid™ (Florbetapir F 18 Injection)

Amyvid is a radioactive diagnostic agent for Positron Emission Tomography (PET) imaging of the brain to estimate beta-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer's Disease (AD) and other causes of cognitive decline.

A negative Amyvid scan indicates sparse to no neuritic plaques and is inconsistent with a neuropathological diagnosis of AD at the time of image acquisition; a negative scan result reduces the likelihood that a patient's cognitive impairment is due to AD. A positive Amyvid scan indicates moderate to frequent amyloid neuritic plaques; neuropathological examination has shown this amount of amyloid neuritic plaque is present in patients with AD, but may also be present in patients with other types of neurologic conditions as well as older people with normal cognition. Amyvid is an adjunct to other diagnostic evaluations.

Limitations of Use:

- A positive Amyvid scan does not establish a diagnosis of AD or other cognitive disorder
- Safety and effectiveness of Amyvid have not been established for:
 - Predicting development of dementia or other neurologic condition
 - Monitoring responses to therapies

Amyvid for intravenous use is supplied in 10 mL, 30 mL, or 50 mL multidose vials containing 500-1900 MBq/mL Florbetapir F 18

WARNINGS AND PRECAUTIONS

Risk for Image Misinterpretation and Other Errors

- Errors may occur in the Amyvid estimation of brain neuritic plaque density during image interpretation
- Image interpretation should be performed independently of the patient's clinical information. The use of clinical information in the interpretation of Amyvid images has not been evaluated and may lead to errors. Other errors may be due to extensive brain atrophy that limits the ability to distinguish gray and white matter on the Amyvid scan as well as motion artifacts that distort the image
- Amyvid scan results are indicative of the brain neuritic amyloid plaque content only at the time of image acquisition and a negative scan result does not preclude the development of brain amyloid in the future

Radiation Risk

- Amyvid, similar to other radiopharmaceuticals, contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk of cancer. Ensure safe handling to protect patients and health care workers from unintentional radiation exposure

MOST COMMON ADVERSE REACTIONS

- The most common adverse reactions reported in clinical trials were headache (1.8%), musculoskeletal pain (0.7%), blood pressure increased (0.7%), nausea (0.7%), fatigue (0.5%), and injection site reaction (0.5%)

For more information about florbetapir F 18, please see the Prescribing Information at <http://pi.lilly.com/us/amyvid-uspi.pdf>.

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About Eli Lilly and Company

Lilly is a global healthcare leader that unites caring with discovery to make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com and newsroom.lilly.com/social-channels. P-LLY

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Lilly Forward-Looking Statement

This press release contains certain forward-looking statements about florbetapir F 18, a radioactive diagnostic agent indicated for brain imaging of beta-amyloid plaques in patients with cognitive impairment who are being evaluated for Alzheimer's Disease and other causes of cognitive decline. This release reflects Lilly's current beliefs; however, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. There is no guarantee that future study results and patient experience will be consistent with study findings to date or that florbetapir F 18 will be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

¹ Pontecorvo M, Siderowf A, Mintun M, et al. A randomized, controlled, multicenter, international study of the impact of florbetapir (¹⁸F) PET amyloid imaging on patient management and outcome. Presented at The Alzheimer's Association International Conference (AAIC) 2015, July 18-23, 2015; Washington, D.C.

² Amyvid [package insert]. Indianapolis, IN: Lilly USA, LLC; 2012.

³ Grundmann, et al. 2013: 31% change in AD drug therapy and 7% change in non AD drug therapy in 229 patients (intended mgmt.).

⁴ Sanchez-Juan et al. 2014: 35% change in cholinesterase inhibitor or memantine use in 140 patients

⁵ Zwan et al. 2014 (abstract) 80 patient study found 20% change in diagnosis and 52% change in patient management (diagnostic studies, drug therapy, and other)

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To view the original version on PR Newswire, visit: <http://www.prnewswire.com/news-releases/new-study-shows-florbetapir-f-18-injection-scans-led-to-change-in-diagnosis-and-management-of-patients-being-evaluated-for-cognitive-decline-300115818.html>

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